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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,274	10/09/2007	Rehab Al-Jamal	MUR-06-1101	9435

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IP GROUP OF DLA PIPER LLP (US)
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EXAMINER	
HADDAD, MAHER M	
ART UNIT	**PAPER NUMBER**
1644	

NOTIFICATION DATE	DELIVERY MODE
10/07/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

pto.phil@dlapiper.com

Office Action Summary	Application No.	Applicant(s)	
	10/576,274	AL-JAMAL ET AL.	
	Examiner	Art Unit	
	MAHER HADDAD	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 May 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1,16,20-24,26,27 and 31-34* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1,16,20-24,26,27 and 31-34* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 05/12/2011, is acknowledged.

2. Claims 1, 16, 20-24, 26-27 and 31-34 are pending and under examination in the instant application.

3. The references with "*" listed on the PTO-892 were provided by Applicant and cited in the Remarks filed 05/12/2011, and will not be supplied.

4. In view of the amendment filed on 05/12/2011, only the following rejections are remained.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1, 16, 20-24, 26, 27 and 31-34 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of promoting tissue repair in lung emphysema comprising administering the monoclonal antibody produced by commercial clone JB1a or antibodies that binds TAEJKJ of SEQ ID NO:1, does not reasonably provide enablement for methods claimed in claims 1, 16, 20-24, 26, 27 and 31-34. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the reasons of record for the reasons set forth in the previous Office Actions.

In addition, the claims now recites "promoting tissue repair" by administering an antibody to "a tissue undergoing cell death".

However, in Parkinson's disease and Alzheimer's disease, tissues undergoing cell death (i.e., neurons) do not repair. There is no regeneration of neurons.

Applicant's arguments, filed 05/12/2011, have been fully considered, but have not been found convincing.

Applicant submits that the specification is not limited to emphysema. Applicant points to the specification and Dr. A.-Jamal's declaration under 1.132, filed 12/28/2009, which contained data demonstrating the JB1a antibody is effective in the treatment *in vivo* of Parkinson's disease and arthritis and Alzheimer's in vitro in art accepted models. This is contrary to the rejection's position that the Applicants have no working examples demonstrating an in vivo treatment

regimen with anti-beta-1 antibodies to promote any tissue repair. Applicant points to the argument on pages 8-9, filed 9/21/2010 regarding the lack of compartmentalization of injury in the lung, the effect of COPD on all tissues and the known association between COPD and other conditions.

However, the specification at [0041] defined the term `tissue repair` relates to repair or regeneration of tissue following damage or trauma. Accordingly, the claims are directed to a genus of tissue repair cause by disease or physical body injury/trauma which encompasses any organ-tissue repairs after injury using anti-TAEKLK antibody, including skin would healing, lung, spinal cord injury, brain trauma, myocardium, parenchyma, stroma, blood, nerve connective tissue, muscle tissue repair, emphysema, Parkinson's, arthritis, Alzheimer's, all types of fibrosis, among others. Applicant's specification is directed to the treatment of emphysema comprising administering the monoclonal antibody produced by commercial clone JB1a. The Declaration provides evidence to treat additional two diseases *in vivo*, Parkinson's disease and arthritis. This is not sufficient to show enablement for the whole genus of tissue repair. Liu et al (J Cell Sci. 2010 Nov 1;123(Pt 21):3674-82) teach that expression of integrin β1 by fibroblasts is required for tissue repair *in vivo*. Importantly, Liu et al teach that the prior art has suggested that expression of integrin β1 by fibroblasts has a key role in cutaneous tissue repair. However, this hypothesis has not yet been tested (see page 3674, last ¶). Liu et al teach that deletion of integrin β1 causes delayed cutaneous wound repair. Integrin-β1-deficient animals showed a significantly reduced rate of wound closure. Integrin-β1-deficient animal displayed reduced collagen production and less granulation tissue (see page 3675, bridging ¶). Liu et al teach that the role of integrin β1 in fibroblasts and myofibroblast-like cells in vivo is largely unknown, as is the precise cell and molecular mechanism underlying integrin β1 action via fibroblasts in tissue repair (see pages 3678-3679, bridging ¶).

It remains the Examiner's position that the Declaration by Dr. Al-Jamal, filed under 37 CFR 1.132 on 12/28/2009 is insufficient to overcome the rejection under 112(1) enablement because the in vivo data do not commensurate with the scope of the claimed invention. The declaration provides data demonstrating that clone JB1a, is effective in the treatment of Parkinson's disease (in vivo data), arthritis (in vivo data), and Alzheimer's (in vitro data), in art accepted models. However, the declaration is limited to the declaration is limited to Parkinson's disease, arthritis and Alzheimer's, however, the claims are directed to any and every tissue repair and tissue injury.

Applicant argues that Grose pertains to the complete deletion of beta-1 integrin, which is not the same as the functional modulation of beta-1 integrin required by the subject matter claimed. In contrast to Grose, the claimed subject matter is neither complete inhibition nor complete activation of beta-1 integrin and which, unlike Grose, does not affect the overall expression level of beta-1 integrin. Secondly, although re-epithelialization eventually occurred, it was largely abnormal with compromised tensile strength, as discussed in page 2312, ¶3. Applicant concluded that complete inhibition of beta-1 integrin resulted in abnormal remodeling rather than

repair. Applicant contends that this does not indicate that beta-1 integrin modulation does not play a role in all tissue repairs.

Again, the claims are drawn to promoting any and every tissue repair including skin wound healing with anti-TAEKLK antibodies. Grose teachings does not address any and every tissue repair, but rather teaches that mutant mice lacking integrin β1 in skin epidermis possessed severe blistering as a result of impaired attachment of basal keratinocytes to the basement membrane, impaired keratinocyte proliferation, dermal fibrosis and severely delayed wound healing (tissue repair). The incomplete inhibition/activation of β1 integrin is immaterial in this instant case because antibodies claimed properties recited in claim 1 do not require partial inhibition/activation of β1 activity. Regarding the second point "re-epithelialization eventually occurred" in the absence of the β1 supports the Examiner's position that β1 integrin is dispensable for re-epithelialization.

Applicant argues that Zweers was focused on the α2 molecule of the α2β1 integrin heterodimer. Applicant concluded that Zweers discloses that α2 is dispensable for re-epithelialization, but does not teach that all β1 integrin receptor types are indispensible for re-epithelialization. β1 integrin was neither manipulated nor altered and the teachings of Zweers are, thus, not related to the subject matter claimed. Applicant concludes that neither Grose nor Zweers show that β1integrin modulation does not play a role in all tissue repairs.

Again, the scope of the claims is not limited to a particular integrin receptor such as α4β1 for reepithelization, but rather generic to any integrin molecule including α2β1 integrin molecule taught by Zweers. Further, the Examiner points to Clark's (of record) finding that fibronectin and fibronectin receptors (e.g., α5β1) are observed to occur in concert during epidermal migration over a wounded surface and may perhaps facilitate migration (see page 133S, 1st col., top ¶). Intervention with this process would inhibit such migration and impair tissue repair.

Applicant argues with respect to the recitation "an alteration in the metalloproteinase balance", applicant argues that the cascading activation of MMPs, which entails lack of association. It is the anti-TAEKLK effect on the cell behavior itself which in turn normalizes MMP activity to that usually present at its physiological baseline. This explains the wide spectrum of indications in which beta-1 integrin targeting has been shown to have efficacy.

It appears that applicant argues that claimed anti-TAEKLK antibody is magic bullet that can result in normalizing all the MMPs, however, Applicant provides no evidence and showing that the claimed anti-TAEKLK antibodies results in normalizing the MMPs balance. Further, given that there is a cascading activation of MMPs, then the effect of the anti-TAEKLK antibody would be on one or two MMPs which would lead to the normalization. It is not clear whether interaction of β1 integrins with their ligands induces/inhibits expression/activation of MMP-1 for example. It is well known known that α2β1 integrin binding will up-regulates expression of MMP-1. α4β1 and α5β1 have been found to have different influences on the expression of three

MMPs in rabbit synoviocytes. Integrin α5β1 increases the expression of MMP-1, MMP-3 and MMP-9, whereas the production of these MMPs is reduced after fibronectin binding via α4β1 integrin (Werb et al. J Cell Biol. 1989;109:877–889). It is not predictable when the anti-TAEKLK antibodies would lead to an increase/decrease in the MMPs expression/activity.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1, 4, 15-16, 20-25, 28-30 stand rejected under 35 U.S.C. 102(b) as being anticipated by US20030109435, as is evidenced by Al-Jamal's declaration, filed 12/28/2009 and Chemicon International catalog no. MAB1965, 9/23/09 (submitted by Applicant on 06/03/2009) for the same reasons set forth in the previous Office Action, mailed 01/13/2011.

Applicant's arguments, filed 05/12/2011, have been fully considered, but have not been found convincing.

Applicant argues that the steps of the claimed process are not the same as the steps described in the `435 publication as the claimed process comprises the step of administering the anti-TAEKLK antibody to a tissue wherein the cells are undergoing cell death whereas the `435 publication teaches administering of the JB1a antibody at an earlier stage where the cells are not yet undergoing cell death. Specifically, the `435 teaches administration of the JB1a antibody to inhibit formation of amyloid deposits.

The Examiner disagrees, the `435 publication explicitly teaches that Parkinson's disease undergoing cell death. In particular, "recent findings suggest that parkin plays an important role in regulating proteins associated with Lewy bodies in the brain, including α-synuclein and synphilin. Normally, parkin uses yet another protein, called ubiquitin, to "tag" other proteins for destruction. But if something goes wrong in the relationship among these proteins, this could lay the groundwork for the cell death seen in Parkinson's disease" [0015].

Moreover, both the instant claims and the `435 publication are directed to a single-action ordering component that in response to performance of only a single action the tissue repair is promoted.

However, the Examiner's position is that `435 publication met the single step method of administering a JB1a antibody that binds to the beta 1 integrin molecule in a region of amino acid residues 82-87 comprising residues TAEKLK which would inherently would result in (i) an

inhibition of the apoptotic pathway, (ii) an alteration in the metalloproteinase balance and (iii) an increase in the anabolism of the extracellular matrix. Even though applicant has recited "a tissue undergoing cell death", Applicant does not appear to distinguish the prior art teaching the same methods steps with the same antibody to treat the same diseases. It is noted that a compound and all of its properties are inseparable; they are one and the same thing (see *In re Papesch*, CCPA 137 USPQ 43; *In re Swinehart and Sfiligoj*, 169) USPQ 226 (CCPA 1971)). Therefore, in the absence of evidence to the contrary, the diseases listed in the `435 publication would inherently undergo cell death.

Applicant's attention is directed to *Ex parte Novitski,* 26 USPQ2d 1389 (Bd. Pat. App. & Inter. 1993) (The Board rejected a claim directed to a method for protecting a plant from plant pathogenic nematodes by inoculating the plant with a nematode inhibiting strain of *P. cepacia.* A U.S. patent to *Dart* disclosed inoculation using *P. cepacia* type Wisconsin 526 bacteria for protecting the plant from fungal disease. Dart was silent as to nematode inhibition but the Board concluded that nematode inhibition was an inherent property of the bacteria. The Board noted that applicant had stated in the specification that Wisconsin 526 possesses an 18% nematode inhibition rating).

Applicant argues that formation of amyloid deposits in neurons takes place before cell death, as ecidenced by Kadowaki et al and Morishima, which show that cell death is cause by, and therefore subsequent to, formation of the amyloid deposits. Applicant submits that the `435 publication teaches administration of the JB1a antibody to inhibit formation of amyloid deposits and, as such, it is necessarily teaches administration of the JB1a antibody at an earlier stage than when the cells are undergoing cell death as, based on the teachings of the US `435, administration of the JB1a antibody would not be beneficial once the cells are undergoing cell death as at the stage amyloid formation has already occurred.

However, the teachings of the `435 publication teaches that "cell death seen in Parkinson's disease" [0015]. Accordingly, by administering the JB1a would inherently be beneficial once the cells are undergoing cell death. Furthermore, in Dr. Al-Jamal's declaration, filed 12/28/2009, with respect to the Parkinson's disease only animal behavior was monitored, no cell death has been show in to occur in the model. That is the criticality of the administration time (before or after amyloid deposits) of the antibody was not necessary to promote tissue repair. It is noted that unilateral injection of 6-OHDA for 3 days would result in significant cell death (i.e., neurons), however, JB1a showed no significant effect.

8. Claims 1, 16 and 21-24 stand rejected under 35 U.S.C. 102(b) as being anticipated by US. Pat. 6,123,941.

Applicant's arguments, filed 05/12/2011, have been fully considered, but have not been found convincing.

Applicant argues that the `941 patent promoting tissue repair by administering an antibody to a tissue undergoing cell death, wherein extracellular matrix of the tissue has been degraded does not include reversing malignant phenotype. Regenerative medicine involving tissue repair is known to be a separate field to cancer as shown in the following references. Listed on http://en.wikipedia.org/wiki/Regenerative_medicine
And
http://en.wikipedia.org/wiki/Regeneration_(biology) and Beachy et al.

Furthermore, malignant tissue is not be considered a tissue undergoing cell death. Applicant submits that the Applicant's claimed subject matter does not include reversing malignant phenotype.

However, the evidence listed by Applicant does not mention any disease that undergo tissue repair, neither lung emphysema, arthritis, Parkinson's disease, Alzheimer's disease nor cancer. There is no limiting definition for "tissue repair" in the specification. The specification discloses that apoptosis is a form of cell death that eliminates compromised or superfluous cells [0020]. Given its broadest reasonable interpretation "tissue repair" can include just lung emphysema, arthritis, Parkinson's disease or Alzheimer's disease but also cancer. The `941 patent teaches that treatment of tumor cells with β1 integrin function-blocking antibody resulted in a significant reduction in basal apoptosis rates of less than 15% suggesting the treatment permitted the tumor cells to respond appropriately to the exogenous basement membrane microenvironment (see example 3, fig. 9).

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over US. Pat. 6,123,941 as in view of Owens *et al* (1994) for the reasons of records.

Applicant's arguments, filed 05/12/2011, have been fully considered, but have not been found convincing.

Applicant argues that Owens does not remedy these argued above deficiencies.

It is the Examiner's position that there are no deficiencies in the primary reference as rebottled above.

11. Claims 1, 16, 20-24 and 31 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US 20070048321, in view of Chen et al, (J. Biol. Chem. 276(13):10443–10452, 2001) for the reasons of record.

Applicant's arguments, filed 05/12/2011, have been fully considered, but have not been found convincing.

Applicant submits that that the `321 and Chen relate to fibrosis. In fibrosis, there is an abnormal increase in matrix anabolism. Thus, treatment of fibrosis differs from the Applicant's claimed subject matter where administration of the antibody to a tissue increases anabolism of extracellular matrix. Applicant concluded that one skilled in the art would not look to the `321 publication or Chen in developing a method of promoting tissue repair comprising administering an antibody, which modulates function of beta 1 integrin, to a tissue undergoing cell death which results in (i) an inhibition of the apoptotic pathway, (ii) an alteration in the metalloproteinase balance and (iii) and increase in the anabolism of the extracellular matrix. Applicant concluded that the `321 and Chen actually teach away from the claimed subject matter because they teach that inhibition of beta 1 integrin will reduce matrix anabolism, whereas increased matrix anabolism is required in tissue repair. Applicant further argues that the `321 describes the use of a beta 1 integrin antibody targeting a sequence in the beta A domain and more specifically, the MIDAS region.

However, it is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. In re Linter, 458 F.2d 1013, 173 USPQ 560 (CCPA 1972) (discussed below); In re Dillon, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1990), cert. denied, 500 U.S. 904 (1991) (discussed below). Although Ex parte Levengood, 28 USPQ2d 1300, 1302 (Bd. Pat. App. & Inter. 1993) states that obviousness cannot be established by combining references "without also providing evidence of the motivating force which would impel one skilled in the art to do what the patent applicant has done " (emphasis added), reading the quotation in context it is clear that while there must be motivation to make the claimed invention, there is no requirement that the prior art provide the same reason as the applicant to make the claimed invention. There is no teaching way in the combined reference teachings. Further, the teachings of the `321 publication is not limited to anti-MIDAS region antibody, but directed to the use of any anti-β1 integrin antibodies.

This is distinct from the TAEKLK sequence in the hybrid region targeted by JB1a. Chen merely describes disruption of the binding of integrins to their ligands using JB1a. Chen, in fact, highlights the importance of activation of metalloproteinases and the interaction of connective tissue growth factor (CTGF) with beta 1 integrin during angiogenesis and wound healing. Chen, therefore, further teaches away from the claimed subject matter because it teaches that inhibition of the interaction between CTGF and beta 1 integrin would detrimental to tissue repair.

However, it remains the Examiner's position that those of skill in the art would have had reason to use the functional-blocking anti-β1 antibody, JB1a of Chen article as a substitute for the treatment taught `321 publication because, like the compounds taught in `321 publication, anti-β1 antibodies inhibit α1β1 or α2β1 ligands, collagen I and IV (see Fig. 1 and 2 of the `321 publication). Functional-blocking antibodies to either of the α1, α2 or β1 would have inhibited the α2β1 ligands interaction. This is pharmaceutical version of the two for the price of one. That is by targeting β1 with JB1a antibody, both α1β1 and α2β1 are inhibited. Substituting a known element for another, to yield the known result, is obvious. See KSR, 550 U.S. at 416, 421.

12. Claims 1, 16 and 20-24 stand rejected under 35 U.S.C. 103(a) as being unpatentable over US. Pat. 6,251,419, in view of Weigel-Kelley et al (Blood. 2003;102:3927-3933, Epub 2003 Aug 7) for the reasons of records.

Applicant's arguments, filed 05/12/2011, have been fully considered, but have not been found convincing.

Applicant argues that Weigel-Kelley teaches that the addition of anti-integrin antibodies was shown to inhibit epithelialization of marginal gingival biopsies comprising epithelium and subepithelium connective tissue. Ephithelialization is a key component of wound healing or wound closure. Weigel-Kelley therefore teaches away from the claimed subject matter because it teaches that inhibition of beta-1 integrin would in fact be detrimental. Furthermore, P4C10 binds the 207-218 amino acid sequence of the beta A domain.

However, it remains the Examiner's position that those of skill in the art would have had reason to use the functional-blocking anti-β1 antibody, JB1a of Weigel-Kelley et al article as a substitute for the treatment taught `419 patent because, like the compounds taught in `419 patent, anti-β1 antibody, JB1a is β1 integrin function-blocking or high-affinity conformation-destabilizing antibody (see Weigel-Kelley et al). Substituting a known element for another, to yield the known result, is obvious. See KSR, 550 U.S. at 416, 421. A person of ordinary skill in the art would have recognized the interchangeability of the element shown in the prior art for the corresponding element recited in the claim.

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 1, 16, 20-24, 26-27 and 31-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 5, 11, 16, 19, 24, 25, 32, 35, 57 and 59-63 of copending Application No. 12528749. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are using the same antibody clone JB1a that binds amino acid residues 82-84 and possible 179-184 (as is evidenced by Al-Jamal and Harrison, Pharmacology & Therapeutics 120 (2008) 81-101, see Table 1) to teat tissue damage.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant submits that because the rejection is provisional, they will address it when the rejection becomes non-provisional.

However, the rejection is maintained until it is addressed.

15. No claim is allowed.

16. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

September 29, 2011

/Maher M. Haddad/
Primary Examiner, Art Unit 1644